

REMARKS

Claims 1, 4-8, 11, 14, 19-21, 24, 28-30 and 35-40 are pending in the present case. In the Office Action dated June 16, 2010, the Examiner maintained rejection of Claims 1, 4-8, 11, 14, 19-21, 24, 28-30, and 35-37 under 35 U.S.C. §103, and rejected new claims 38-40 under the same section, as allegedly being unpatentable over Lapidus, *et al.*, (US 6,143,529; 11/7/00) in view of Hromadnikova et al (BMC Pregnancy and Childbirth, 5/28/02, 2(4):1-5). Applicants disagree with the maintained rejections for the reasons made of record in the response filed on June 1, 2010, which are incorporated here by reference. However, for business reasons and without acquiescing to the Examiner's arguments, and reserving the right to prosecute the original or similar claims in one or more future applications, independent claims 1, 14, and 24 are herein amended to recite that the nucleic acid fragments measured are "amplified from heterogeneous DNA from a stool sample, said stool sample comprising DNA from shed cells and shed cellular debris." Support for this amendment is found, *e.g.*, in Example 1, which describes the isolation of unfractionated DNA from stool samples in paragraph [0059], and describes PCR amplification from this total DNA in paragraph [0060].

Nowhere does Lapidus teach or suggest analysis of DNA fragments amplified directly from heterogeneous DNA. Rather, Lapidus particularly emphasizes the difficulty of detecting cancer indicia in the heterogeneous environment of a stool sample. As noted in column 1 of Lapidus, a typical stool sample contains cells and cellular debris sloughed from the colonic epithelium and bacteria, along with by-products of digestion. (Lapidus col 1, lines 65-67), making stool samples a source of highly heterogeneous DNA. As Lapidus further points out, "simply obtaining adequate human DNA from one type of heterogeneous sample (stool) has proven difficult. See Villa, et al., Gastroenterol., 110: 1346-1353 (1996) (reporting that only 44.7% of all stool specimens, and only 25 32.6% of stools from healthy individuals produced sufficient DNA for mutation analysis)." See Lapidus at col 2, lines 21-26.

In view of these difficulties, Lapidus teaches that the DNA to be analyzed is first purified from the stool samples (see, *e.g.* col 10, lines 18-28.) The human DNA to be

amplified is then further purified by fractionation from the heterogeneous population of molecules *by sequence-specific hybrid capture* prior to the amplification step. See, e.g., col 10 lines 29-30. Lapidus does not disclose amplification directly from the unfractionated, heterogeneous collection of nucleic acids isolated from stool.

The Examiner asserts that the deficiency in Lapidus with respect to measurement of genome equivalents is made up in the teachings of Hromadnikova *et al.* (Office Action, page 5). While Hromadnikova does teach determination of "genome equivalents", the teachings of Hromadnikova are not sufficient to make up for all of the deficiencies of Lapidus discussed above. Hromadnikova fails to teach or suggest a method comprising the step of amplifying from the heterogeneous DNA isolated from a stool sample, the stool sample comprising DNA from shed cells and shed cellular debris." As such, even if the teachings of Hromadnikova are combined with the teachings of Lapidus (Applicants do not concede that such a combination is proper or would be made by one of skill in the art), the combination fails to teach or suggest each and every feature of the instant claims.

It remains well-settled law that obviousness requires at least a suggestion of all of the features in a claim. Section 2143.03 of the MPEP, citing *See In re Wada and Murphy*, citing *CFMT, Inc. v. Yieldup Intern. Corp.*, 349 F.3d 1333, 1342 (Fed. Cir. 2003) and *In re Royka*, 490 F.2d 981, 985 (CCPA 1974)). While Applicants do not acquiesce that the other elements necessary for establishing prima facie obviousness have been met, Applicants submit that the combination of Lapidus and Hromadnikova does not teach or suggest all the features of Claims 1, 4-8, 11, 14, 19-21, 24, 28-30 and 35-40, and cited art therefore fails to establish prima facie obviousness. Applicants respectfully request that this rejection be withdrawn.

CONCLUSION

For the reasons set forth above, it is respectfully submitted that all grounds for rejection have been addressed and Applicants' claims should be passed to allowance. If the Examiner wishes to discuss this case, Applicants encourage the Examiner to call the undersigned at 608-662-1277 at the Examiner's convenience.

Dated: October 18, 2010

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